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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,550	06/28/2001	Albert Collinson	BBC-083 A US	6240

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KENNETH P. ZWICKER
ABBOTT BIORESEARCH CENTER
100 RESEARCH DRIVE
WORCESTER, MA 01605

EXAMINER	
ANDRES, JANET L	

ART UNIT	PAPER NUMBER
1646	15

DATE MAILED: 10/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/894,550	COLLINSON ET AL.	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-95* is/are pending in the application.

4a) Of the above claim(s) *5-8,11 and 32-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,12-31 and 89-95* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 30 June 2003 is acknowledged. Claims 1-95 are pending in this application. Claims 5-8, 11, and 32-88 are withdrawn from consideration as being drawn to a non-elected invention. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

2. The objection to the specification is withdrawn in response to Applicant's amendment.

3. The rejection of claims 1-4, 12-14, and 31 under 35 U.S.C. 102(b) as anticipated by Luger et al. is withdrawn in response to Applicant's amendment limiting the claims to antibodies that are not fully mouse.

4. The rejection of claims 9 and 31 under 35 U.S.C. 112, 2nd paragraph, as indefinite is withdrawn in response to Applicant's amendment to these claims.

Claim Rejections Maintained/New Grounds of Rejection

5. The rejection of claims 16-30 under 35 U.S.C. 103(a) as unpatentable over Luger et al. in view of Green, Nguyen et al., Reisner et al., Barbas et al., WO 99/36569, WO 98/49286, WO 98/31700, US 5580717, WO 97/29131, Babcock et al., or Knappik et al. is maintained for reasons of record in the office action of paper no. 13 and newly applied to amended claims 1-4, 12-14, and 31 and new claims 89-95.

Applicant argues that Luger et al. does not teach the use of transgenic animals (p. 9), SCID mice (p. 10), irradiation of SCID mice and reconstitution (p. 11), screening of libraries (pp. 12 and 13), recombinant antibody libraries (p. 15), *in vitro* affinity maturation (p. 15), selection of single cells (p. 17), or chimeric or CDR-grafted antibodies (p. 17). Applicant additionally

argues that the references citing these methodologies do not teach dually-reactive antibodies. (pp. 9-17). Applicant concludes that the references, together or separately, do not teach Applicant's invention and further argues that hindsight reasoning has been used.

Applicant's arguments have been fully considered but have not been found to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The combination of references does teach Applicant's invention, for the reasons set forth in the office action of paper no. 13. Luger et al. teaches an antibody with particular characteristics. Green, Nguyen et al., Reisner et al., Barbas et al., WO 99/36569, WO 98/49286, WO 98/31700, US 5580717, WO 97/29131, Babcock et al., and Knappik et al. each teach modifications or approaches to making antibodies that, combined with the teachings of Luger et al., lead one of ordinary skill in the art to Applicant's claimed invention. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, no knowledge other than that of the antibody of Luger et al. and the techniques taught by the other cited references is required. Motivation to combine the references is, as stated previously, provided by the teachings of Luger et al. that the antibody inhibits a molecule involved in inflammation, and the teachings of the other references as to how to make antibodies with improved characteristics. The rejection thus takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only

from the applicant's disclosure. Such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

6. The rejection of claims 1-4, 9, and 12-31 under 35 U.S.C. 112, first paragraph, as lacking enablement commensurate with the scope of the claims is maintained for reasons of record in the office action of paper no. 13 and applied to new claims 89-95.

Applicant argues that Applicant teaches how to make antigens on pp. 7-11 and 47-49 of the specification, how to make antibodies on pp. 11-31, and how to screen for them on pp. 31-33. Applicant argues that sufficient guidance is provided so that only a reasonable number of peptides need to be screened, and that a working example is provided.

Applicant's arguments have been fully considered but have not been found to be persuasive. While a general discussion of various approaches to the generation of antigens is provided, as well as general techniques for the making and screening of antibodies, what is provided that is specific to IL-1α and IL-1β are four peptides, examples of the various general approaches taught by Applicant. See pp. 47-49. Of these, three peptides failed to generate dually specific antibodies. See p. 49, lines 16-19: "However, only antiserum from rabbit immunized with Peptide of SEQ ID NO: 3 was able to bind both IL-1α protein and IL-1β protein." These peptides exemplified the different types of regions taught by Applicant as being useful; thus, peptides designed following the guidance in the specification failed to generate the desired antibody in three of the four approaches exemplified. Thus, as stated previously, Applicant has not described the characteristics of the peptides that generate the desired antibodies. While, as Applicant states, inoperative embodiments are allowed, and extensive experimentation is not necessarily undue, the specification does not, based on Applicant's own

results, provide guidance sufficient to allow an expectation of a successful outcome on the part of the artisan.

7. Claims 4, 12-15, and 19-24 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making antibodies that are not fully mouse *in vitro*, in transgenic or irradiated mice, and in animals other than mice, does not reasonably provide enablement for the methods as they broadly encompass mouse-generated antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

These claims require that the antibodies be not fully mouse, but encompass standard methods of generating monoclonal polyclonal and monoclonal antibodies in mice. Unless the mouse or the antibody produced is altered in some way, the resulting antibodies are fully mouse antibodies. Thus the claims encompass methods of generating not fully mouse antibodies that would of necessity result in fully mouse antibodies, and the artisan would be unable to make and use the invention as broadly claimed.

Allowable Subject Matter

8. Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

CLAIMS 1-4, 9, 12-31, AND 89-95 ARE REJECTED. CLAIM 10 IS OBJECTED TO.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that

sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
October 6, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600